

amino acid addition, substitution, and/or deletion in the B domain corresponding to amino acid residues 495-535 of a wild-type HBV polymerase, and said mutant contains an unmutated YMDD motif in the C domain.

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56. (Amended) An isolated HBV mutant, comprising a mutation in the gene encoding the HBV DNA polymerase resulting in decreased sensitivity to a nucleoside analogue compared to a wild-type HBV, wherein said mutation results in at least one amino acid addition, substitution, and/or deletion in the B domain corresponding to amino acid residues 505-535 of a wild-type HBV polymerase, and said mutant contains an unmutated YMDD motif in the C domain.

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57. (Amended) An isolated HBV mutant, comprising a mutation in the gene encoding the HBV DNA polymerase resulting in decreased sensitivity to a nucleoside analogue compared to a wild-type HBV, wherein said mutation results in at least one amino acid addition, substitution, and/or deletion in the B domain corresponding to amino acid residues 505-529 of a wild-type HBV polymerase, and said mutant contains an unmutated YMDD motif in the C domain.

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58. (Amended) The HBV mutant according to any of claims 55 or 56 wherein said mutation is selected from the group consisting of Arg/Trp499Glu, Phe512Leu, Val519Leu, Pro523Leu, Leu526Met, Thr530Ser, and Ile533Leu.

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59. (Amended) The HBV mutant according to claim 58 wherein said mutation is selected from the group consisting of Arg/Trp499Glu, Phe512Leu, Val519Leu, Pro523Leu, Leu526Met, Thr530Ser, and Ile533Leu.

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60. (Amended) An isolated HBV mutant exhibiting, relative to an isolated wild-type HBV, reduced sensitivity to a nucleoside analogue, said mutant comprising at least one mutation in its genome wherein said at least one mutation produces at least one

amino acid substitution in the DNA polymerase selected from the group consisting of Trp/Arg499Glu, Phe512Leu and Val519Leu, said amino acid substitution in the DNA polymerase resulting in a concurrent amino acid substitution in the overlapping open reading frame of the HBV surface antigen, and said mutant contains an unmutated YMDD motif in the C domain.

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cont.
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68. (Amended) An isolated HBV mutant exhibiting, relative to an isolated wild-type HBV, reduced sensitivity to a nucleoside analogue, said mutant comprising at least one mutation in its genome wherein said at least one mutation produces at least one amino acid substitution in the DNA polymerase selected from the group consisting of Trp/Arg499Glu, Phe512Leu, Val519Leu and Ser559Thr, said amino acid substitution in the DNA polymerase resulting in a concurrent amino acid substitution in the overlapping open reading frame of the HBV surface antigen, and said mutant contains an unmutated YMDD motif in the C domain.

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74. (Amended) An isolated *Hepadnavirus* mutant, comprising a mutation in the gene encoding the DNA polymerase, resulting in decreased sensitivity to a nucleoside analogue compared to a wild-type *Hepadnavirus*, wherein said mutation results in at least one amino acid addition, substitution, and/or deletion in the B domain corresponding to amino acid residues 495-535 of a wild-type HBV polymerase, and said mutant contains an unmutated YMDD motif in the C domain.

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75. (Amended) An isolated *Hepadnavirus* mutant, comprising a mutation in the gene encoding the DNA polymerase, resulting in decreased sensitivity to a nucleoside analogue compared to a wild-type *Hepadnavirus*, wherein said mutation results in at least one amino acid addition, substitution, and/or deletion in the B domain corresponding to amino acid residues 505-535 of a wild-type HBV polymerase, and said mutant contains an unmutated YMDD motif in the C domain.